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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/866,538	05/24/2001	Roger Y. Tsien	REGEN1530-2	4548

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EXAMINER

KAM, CHIH MIN

ART UNIT	PAPER NUMBER
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1653

DATE MAILED: 02/20/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Advisory Action</b>	<b>Application No.</b> 09/866,538	<b>Applicant(s)</b> TSIEN ET AL.	
	<b>Examiner</b> Chih-Min Kam	<b>Art Unit</b> 1653	

**--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --**

THE REPLY FILED 30 January 2004 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE. Therefore, further action by the applicant is required to avoid abandonment of this application. A proper reply to a final rejection under 37 CFR 1.113 may only be either: (1) a timely filed amendment which places the application in condition for allowance; (2) a timely filed Notice of Appeal (with appeal fee); or (3) a timely filed Request for Continued Examination (RCE) in compliance with 37 CFR 1.114.

**PERIOD FOR REPLY** [check either a) or b)]

- a) ☒ The period for reply expires 6 months from the mailing date of the final rejection.
- b) ☐ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection. **ONLY CHECK THIS BOX WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).**

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

1. ☐ A Notice of Appeal was filed on \_\_\_\_\_. Appellant's Brief must be filed within the period set forth in 37 CFR 1.192(a), or any extension thereof (37 CFR 1.191(d)), to avoid dismissal of the appeal.
2. ☒ The proposed amendment(s) will not be entered because:
- (a) ☐ they raise new issues that would require further consideration and/or search (see NOTE below);
  - (b) ☐ they raise the issue of new matter (see Note below);
  - (c) ☒ they are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or
  - (d) ☐ they present additional claims without canceling a corresponding number of finally rejected claims.

NOTE: See Continuation Sheet.

3. ☒ Applicant's reply has overcome the following rejection(s): See Continuation Sheet.
4. ☐ Newly proposed or amended claim(s) \_\_\_\_\_ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).
5. ☒ The a) ☐ affidavit, b) ☐ exhibit, or c) ☒ request for reconsideration has been considered but does NOT place the application in condition for allowance because: See Continuation Sheet.
6. ☐ The affidavit or exhibit will NOT be considered because it is not directed SOLELY to issues which were newly raised by the Examiner in the final rejection.
7. ☒ For purposes of Appeal, the proposed amendment(s) a) ☒ will not be entered or b) ☐ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.

The status of the claim(s) is (or will be) as follows:

Claim(s) allowed: \_\_\_\_\_.

Claim(s) objected to: \_\_\_\_\_.

Claim(s) rejected: 88,93-99,102-110,128,134 and 138.

Claim(s) withdrawn from consideration: \_\_\_\_\_.

8. ☐ The drawing correction filed on \_\_\_\_\_ is a) ☐ approved or b) ☐ disapproved by the Examiner.
9. ☐ Note the attached Information Disclosure Statement(s) (PTO-1449) Paper No(s). \_\_\_\_\_.
10. ☒ Other: See Continuation Sheet

Continuation of 2. NOTE: The amendment to the claims does not resolve the current issues under 35 USC 112, first paragraph. In the amendment of January 30, 2004, claims 88 and 96 have been amended, claims 93-95 and 97 have been cancelled, and new claims 154-156 have been added. Applicants' response has been fully considered, however, claims 96, 98 and 154-156 are rejected under 35 USC 112, first paragraph.

If applicants' amendment were entered, it would have the following response:

1. Claims 96, 98 and 154-156 are rejected under 35 USC 112, first paragraph, because the specification, while being enabling a polynucleotide encoding at least a first monomer of a non-oligomerizing tandem fluorescent protein, wherein the fluorescent protein comprises a first monomer of an Aequorea GFP or a fluorescent protein related to Aequorea GFP operatively linked to at least a second monomer of an Aequorea GFP or a fluorescent protein related to an Aequorea GFP, wherein the amino acid sequence of the first monomer is defined (e.g., A206K, L221K or F223R mutant of SEQ ID NO:6 or 10), and wherein the propensity of the tandem fluorescent protein to form intermolecular oligomer is reduced or inhibited; a vector or a host cell comprising the polynucleotide; a kit comprising the polynucleotide, does not reasonably provide enablement for a polynucleotide encoding at least a first monomer of a non-oligomerizing tandem fluorescent protein, wherein the fluorescent protein comprises a first monomer of an Aequorea GFP or a fluorescent protein related to an Aequorea GFP operatively linked to at least a second monomer of an Aequorea GFP or a fluorescent protein related to an Aequorea GFP, wherein the first monomer "further comprises" a mutation substituting an amino acid having a positively charged side-chain for amino acid corresponding to A206, L221, F223 or a combination thereof of SEQ ID NO:2, but the sequence of first monomer is not defined, and wherein the propensity of the tandem fluorescent protein to form intermolecular oligomer is reduced or inhibited; a vector or a host cell comprising the polynucleotide; a kit comprising the polynucleotide. The specification indicates the specific A206K, L221K and F223R mutants of SEQ ID NOs:6 and 10 are non-oligomerizing fluorescent protein (Example 1), it does not demonstrate the make/use of a first monomer of a non-oligomerizing tandem fluorescent protein, which comprises an Aequorea GFP or a fluorescent protein related to Aequorea GFP, and further comprises a mutation at A206, L221, F223 of SEQ ID NO:2, being linked to a second monomer of an Aequorea GFP or a fluorescent protein related to an Aequorea GFP, nor shows the effects of reducing oligomerization in these tandem fluorescent proteins, while the claims encompass the polynucleotides encoding these first monomer. Since the specification does not provide sufficient teachings regarding these monomers, it is necessary to have further experimentation to assess the effects of these monomers in the non-oligomerizing tandem fluorescent proteins. In response, applicants indicate claim 96 has been amended to cite the first monomer comprising a mutation substituting an amino acid having a positively charged side-chain for amino acid corresponding to A206, L221, F223 or a combination thereof of SEQ ID NO:2, which has been described as being enabled in the Office Action (page 8 of the response). The response has been fully considered, however, the argument is not found persuasive because the claim cites a first monomer of an Aequorea GFP or a fluorescent protein related to an Aequorea GFP "further comprises" the mutation of SEQ ID NO:2, it does not identify what amino acid sequence the first monomer has in addition to the mutation of SEQ ID NO:2.

Continuation of 3. Applicant's reply has overcome the following rejection(s): If entered, the rejection of claims 88, 99, 102-110, 128, 134 and 138 under 35 USC 112, first paragraph; and claims 88, 99, 102-110, 128 and 134 under 35 USC 102.

Continuation of 5. does NOT place the application in condition for allowance because: the amendment to the claims does not resolve current issue under 35 USC 112, first paragraph for claims 96, 98 and 154-156.

Continuation of 10. Other: It is noted that SEQ ID NO:2 has 238 amino acids, and SEQ ID NOs:6 and 10 have 239 amino acids, where A206 in SEQ ID NO:2 corresponds to A207 in SEQ ID NOs:6 and 10.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Chih-Min Kam whose telephone number is (571) 272-0948. The examiner can normally be reached on 8.00-4:30, Mon-Fri.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low can be reached on (571) 272-0951. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 872-9306 for regular communications and (703) 308-4227 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.

Chih-Min Kam, Ph. D.  
Patent Examiner

*CMK*

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February 14, 2004.

*Christopher S. F. Low*  
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